REMARKS

Reconsideration is respectfully requested. The present communication is in response to the Office Action dated July 10, 2007. Claims 1-14 and 36-42 are canceled. Claims 15, 21, 22 and 26 are amended. Claims 43-45 are new. Claims 15-35 and 43-45 are pending.

As per the Examiner's suggestion, claim 26 has been amended to correct the typographical error. Support for amended claim 15 may be found, for example, in the specification at paragraph 0067. Support for amended claim 21 may be found, for example, in the specification at paragraphs 0018-0019 and 0078-0087. Support for amended claim 22 may be found, for example, in the specification at paragraph 0090 and in Example 4, at paragraph 0144. Support for new claims 43-45 may be found, for example, in the specification at paragraph 0067 and at paragraph 0090. No new matter has been added.

Applicant has not dedicated or abandoned unclaimed subject matter, and has not acquiesced to any rejections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

In view of the following remarks, Applicant respectfully requests reconsideration and allowance of the pending claims.

Rejection under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected Claim 26 under 35 U.S.C. § 112, Second Paragraph, stating that it is vague and indefinite what is meant by the "15" preceding the term "polystyrene". Applicant has amended claim 26 to delete the 15 and this ground for rejection is therefore moot and should be withdrawn.

Rejections under 35 U.S.C. § 102

The Examiner has rejected claims 15-19, 22-24, and 32-35 under 35 U.S.C. § 102(b) on multiple grounds. Applicant respectfully traverses the rejections for at least the following reasons.

1. Asada does not teach a kit for polynucleotide synthesis wherein a non-nucleic acid polyanion is combined with a thermostable polymerase to inhibit DNA synthesis in a temperature dependent manner, as required by claim 15.

Claims 15-19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Asada et al., WO 00/14218, which is published in Japanese, and therefore U.S. Patent No. 6,673,578 to Uemori et al. is being used as the English translation, as per the Office Action, page 4, paragraph 1 (hereinafter "Asada").

Asada does not teach or suggest a kit for polynucleotide synthesis comprising a polymerase, a non-nucleic acid polyanion, at least 1.5 mM magnesium and between about 35 and 100 mM monovalent cations with instructions to combine the non-nucleic acid polyanion and polymerase to inhibit DNA synthesis in a temperature dependent manner. To the contrary, Asada teaches directly the opposite: the laundry list of acidic substances disclosed by Asada are included in the kit and added to their PCR reagent mixture for the opposite purpose of enhancing DNA synthesizing activity:

> Regarding the preparation of the PCR reagent mixture, the kit of the present invention encompasses a kit to which instructions for use of the amount of the above DNA polymerase and/or the addition of the above acidic substance or a salt thereof are attached. . . . The kit may contain an acidic substance or a salt thereof possessing an action of enhancing DNA-synthesizing activity of the DNA polymerase.

[col. 13, lines 3-12]. Asada repeatedly teaches that their so-called acidic substances are added for the purpose of enhancing the DNA-synthesizing activity of the polymerase, and that modified forms of such substances can be used so long as they possess an action of enhancing DNA-synthesizing activity. [cols. 8-11 and 13]. Asada also exemplifies the enhancement of Taq DNA polymerase-synthesizing activity by an acidic substance in Example 5. As such, the kit disclosed by Asada would clearly not include instructions to combine a non-nucleic acid polyanion with a polymerase to inhibit DNA synthesis in a temperature-dependent manner. Rather, the Asada kit includes directly contrary instructions.

Claim 15 as amended requires a kit including instructions to combine the polyanion and polymerase for the purpose of inhibiting DNA synthesis in a temperature dependent manner, a feature which is not found in Asada and is directly contrary to their teaching. As discussed in the present specification, "the invention is based upon, among other things, a temperature dependent inhibition of thermostable polymerases during polynucleotide synthesis. In particular, the invention provides for increased sensitivity and specificity of polynucleotide synthesis techniques by reversibly inhibiting thermostable polymerases with non-nucleic acid polyanions. Inhibition of the thermostable polymerase is temperature dependent: at ambient temperatures, i.e., below the specific annealing temperature of the primers used in the polynucleotide synthesis reaction, the non-nucleic acid polyanion competitively inhibits the thermostable polymerase from binding and extending any non-specific primer/template complexes. At elevated temperatures, i.e., above the specific annealing temperature of the primers used in the polynucleotide synthesis reaction, the non-nucleic acid polyanion no longer acts as a competitive inhibitor of the thermostable

polymerase." [0067, emphasis added]. New claim 48 further specifies instructions to preincubate the polymerase and polyanion in the reaction mixture at ambient temperature before adding template nucleic acid and appropriate primers, which again clearly distinguishes over Asada. Since the instructions in Asada are directly contrary this reference and cannot anticipate the kit as presently claimed, Applicant respectfully requests that this rejection be withdrawn.

2. Asada does not teach a pre-inhibited thermostable polymerase composition for polynucleotide synthesis comprising a thermostable polymerase and a non-nucleic acid polyanion in a storage buffer

Claims 22 and 32-34 are also rejected under 35 U.S.C. § 102(b) as being anticipated by Asada. The Examiner states that Asada teaches a composition comprising a thermostable polymerase, a non-nucleic acid polyanion and a polymerase reaction buffer and etc. (Office Action page 5, paragraph 5). Claim 22, in contrast, is directed to a pre-inhibited thermostable polymerase composition comprising a thermostable polymerase and a non-nucleic acid polyanion in a storage buffer, as disclosed at paragraph 0090 and in Example 4 of Applicant's specification. Asada does not teach or suggest such a composition and therefore cannot anticipate the composition as presently claimed, nor can Asada anticipate kits comprising such a composition as set forth in new claims 43-47.

In particular, Asada does not teach the preparation of a polymerase storage buffer nor does it teach adding a non-nucleic acid polyanion to such a buffer. Rather, the Examiner admits that Asada teaches the preparation of a polymerase reaction buffer. (Office Action page 5, paragraph 5). The Examiner refers to col. 20, lines 59-62 in which Asada teaches components of a reaction buffer. Asada further states, "[t]he above DNA polymerase, the acidic substance and other reagents may be contained in a state where each is present as an independent component, or a state in which some of the components are combined, including, for instance, a state in which the components are added to the reaction buffer and the like." (col. 13, lines 34-39). Thus, Asada teaches reagents for a reaction mixture and the addition of the acidic substance to the reaction mixture (buffer). Asada provides no teaching or suggestion of a pre-inhibited polymerase composition in a storage buffer.

Further, a pre-inhibited thermostable polymerase composition or kit comprising the same is not inherent in the teachings of Asada. As the Examiner is well aware, "the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *Id.* (quoting *In re Oelrich*, 212 USPQ 323, 326 (CCPA 1981)). In order to make a *prima facie* case of inherent anticipation based on the cited reference, the Examiner is required to advance a basis in fact and/or technical reasoning to reasonably support the assertion that the presently claimed invention

necessarily flows from Asada. A pre-inhibited thermostable polymerase composition and kits comprising the same certainly do not necessarily flow from the teachings of Asada, since Asada is actually focused on the opposite functionality, i.e., the enhancement of polymerase activity. It clearly does not flow from Asada that one would instead pre-inhibit a polymerase by combining it with a polyanion in the polymerase storage buffer. Thus, Asada cannot inherently anticipate the composition or kits as presently claimed.

Asada therefore does not anticipate claim 22 or its dependent claims 23-35, or new kit claims 43-47. Applicant respectfully requests that this rejection be withdrawn.

3. Schinazi does not teach or suggest the pre-inhinited polymerase composition as presently claimed

The Examiner has rejected claims 22-29, 32 and 35 under 35 U.S.C. § 102(b) as being anticipated by Schinazi et al., Antimicrobial Agents and Chemotherapy, 1989, vol. 33, no 1, pp. 115-117, (hereinafter "Schinazi").

Schinazi does not teach a pre-inhibited thermostable polymerase composition or a kit comprising said composition. The Examiner states Schinazi teaches a composition comprising a thermostable polymerase, a non-nucleic acid polyanion, a polymerase reaction buffer and etc. (Office Action, page 6, paragraph 2). The Examiner generally refers to Table 1 and its caption. (*Id.*) As described therein Schinazi tested and compared several known antiretroviral agents for their ability to inhibit the activities of HIV-1 RT purified from two different sources, by combining them in a standard reaction mixture. (Abstract, col.1, paragraph 1). Thus, Schinazi was concerned solely with a comparison of inhibitory activities of various compositions from a potential therapeutic perspective and provides no teaching or suggestion whatsoever for the preparation of a pre-inhibited thermostable polymerase or a kit comprising said composition as presently claimed.

Further, a pre-inhibited thermostable polymerase composition or a kit comprising said composition is not inherent in the teachings of Schinazi. To satisfy the requirements of inherent anticipation, a teaching must necessarily flow from the cited reference. A pre-inhibited thermostable polymerase composition certainly does not flow from Schinazi, which is concerned with assaying for potentially therapeutic compositions as opposed to preparing pre-inhibited thermostable polymerase compositions for use in polynucleotide synthesis.

Because Schinazi does not teach a pre-inhibited thermostable polymerase composition or a kit comprising said composition, claims 22-25, and 43-47 are not anticipated. Applicant respectfully requests that this rejection be withdrawn.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 15, 17-32, and 35 under 35 U.S.C. § 103(a) on multiple grounds. Applicant respectfully traverses the rejections for at least the following reasons.

1. The combination of Ueno and the Stratagene Catalog does not render obvious a kit for polynucleotide synthesis as presently claimed

Claims 15 and 17-21 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ueno et al., U.S. Patent No. 4,840,941 (hereinafter "Ueno") in view of the 1988 Stratagene Catalog (hereinafter "the Stratagene Catalog").

To satisfy the requirements of a *prima facie* case for obviousness, the cited references must teach every limitation of the claimed invention.

Ueno does not teach or suggest a kit for polynucleotide synthesis wherein a non-nucleic acid polyanion and a thermostable polymerase are combined to inhibit DNA synthesis in a temperature dependent manner. To the contrary, Ueno is concerned solely with potential therapeutic aspects of enzyme inhibitors and therefore provides no teaching or suggestion whatsoever of a kit for polynucleotide synthesis, as the Examiner has acknowledged. (Office Action page 8, paragraph 2).

The Stratagene Catalog, in contrast, is directed to clearly divergent subject matter from Ueno and is therefore not properly combinable with Ueno in the first instance. Moreover, even if improperly combined the Stratagene Catalog disclosure fails to make up for the shortcomings of Ueno. The Examiner states the Stratagene Catalog provides a general motivation to combine reagents into kit format. (Office Action page 8, paragraph 3). However, the Stratagene Catalog does not teach or suggest a kit with instructions to combine a non-nucleic acid polyanion with a thermostable polymerase to inhibit DNA synthesis in a temperature dependent manner, a teaching which is also clearly absent in Ueno. Accordingly, because neither Ueno nor the Stratagene Catalog teach every limitation of claim 15 or dependent claims 16-21 and 48, said claims are patentable over Ueno in view of the Stratagene Catalog. Applicant respectfully requests that this rejection be withdrawn.

2. Diringer and Jurkiewicz do not teach or suggest a pre-inhibited thermostable polymerase composition for polynucleotide synthesis as presently claimed

Claims 22-32 and 35 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Diringer et al., U.S. Patent No. 5,153,181, (hereinafter "Diringer") in view of Jurkiewicz et al., AIDS, 1989, vol. 3, pp. 423-427, (hereinafter "Jurkiewicz").

To satisfy the requirements of a *prima facie* case for obviousness, the cited references must teach every limitation of the claimed invention.

Diringer does not teach or suggest the pre-inhibited thermostable polymerase composition of claim 22. Diringer teaches the use of organic polymers which contain inorganic anionic groups for prophylaxis and therapy of retrovirus infections in mammals. (Abstract). Diringer further describes its therapeutic objective as providing inhibitors of reverse transcriptase which in comparison to the known inhibitors of this enzyme exhibit less side effects on the mammalian organism. (col. 2, lines 29-35). The Examiner states that Diringer was performing assays and testing various polyanionic compounds for their effects on HIV reverse transcriptase. (Office Action page 10, paragraph 5). However, Diringer clearly does not teach or suggest the preparation and/or use of a pre-inhibited thermostable polymerase composition in a storage buffer as presently claimed.

Jurkiewicz does not compensate for the failings of Diringer. Jurkiewicz states that the purpose of its study was to examine whether chondroitin polysulphate has an appreciable *in vitro* effect against HIV and its reverse transcriptase and to compare it with a group of related substances and zidovudine. (col. 1-2, rollover paragraph). The Examiner states that Jurkiewicz was performing the same types of assays as Diringer. (Office Action, page 10, paragraph 5; see also immediately preceding paragraph of this response). However, Jurkiewicz also does not teach or suggest a pre-inhibited thermostable polymerase composition in a storage buffer as presently claimed.

As discussed in the specification and above, claim 22 requires a storage buffer. Jurkiewicz is cited for teaching a reaction buffer for HIV reverse transcriptase comprising 30mM KCl. (Office Action page 10, paragraph 5). Jurkiewicz does not teach a storage buffer. Thus, Jurkiewicz also does not teach every limitation of claim 22.

Therefore, because neither Diringer nor Jurkiewicz teaches every limitation of claim 22, with the further limitations of claims 23-35 and 43-47, said claims are patentable over Diringer in view of Jurkiewicz. Applicant respectfully requests that this rejection be withdrawn.

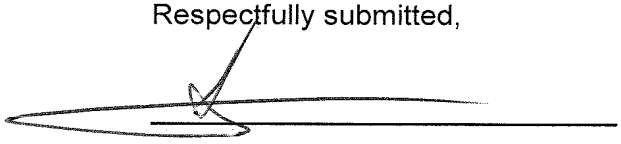
Conclusion

Applicant respectfully submits that this application now stands in allowable form and reconsideration and allowance is respectfully requested.

This response is being submitted on or before December 10, 2007, along with the required fee, and a two month extension of time making this a timely response. It is believed that no additional fees are due in connection with this filing. However, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment and notify us of same, to Deposit Account No. 502319 (Our file 469981-00065).

Dated this 10th day of December 2007.

Respectfully submitted,



Todd A. Lorenz, Reg. No. 39,754

Customer Number: 32940
Dorsey & Whitney LLP
Intellectual Property Department
555 California Street, 3rd Floor
San Francisco, CA 94104-1513
Telephone: (415) 568-2253
Facsimile: (415) 398-3249

TAL/KMK/dtc